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FILE COVERS 1967 - 20 Sep 1999 VOL 131 ISS 13
FILE LAST UPDATED: 20 Sep 1999 (19990920/ED)

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=> s review/dt

L1 1331380 REVIEW/DT
=> s (cell?)(therap?)?/ab,bi

1883075 CELL?
139989 (THERAPY)/AB
179421 (THERAPY)/BI
L2 7686 (CELL?)(SAXTHERAPY)/AB,BI
=> s l1 and l2

L3 1401 L1 AND L2
=> s (cell?)(therap?)?/ab,bi

1883075 CELL?
139989 (THERAPY)/AB
179421 (THERAPY)/BI
L4 4796 (CELL?)(SAXTHERAPY)/AB,BI

toxic drugs will appear. There are some coadjutant drugs which can be employed, and others useful in the control of psychotic and depressive symptoms.

Even though we cannot yet talk of effective and attainable treatments at this moment, but we can hope that new drug ***administration*** routes and pharmacol. approaches (brain injections, slow drug diffusion pumps, ***neuron*** and glial ***cell*** implants, and gene ***therapy***) will, in the near future, be able to control the evolution of the illness.

=> s l4 and neuro?/ab,bi
227772 NEURO?/AB
301028 NEURO?/BI
L8 277 L4 AND NEURO?/AB,BI
=> d bib ab
L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
AN 1997333476 CAPLUS
DN 1261338287
TI Theories and new therapeutics to cure Alzheimers disease
AU Toledoano, Adolfo
CS Inst. Cajal C.S.I.C., Madrid, Spain
SO An. R. Acad. Farm. (1996), 62(4), 71-765
CODENI: ARAFAY, ISSN: 0034-0618
PB Real Academia de Farmacia
DT Journal: ***General Review***
LA Spanish
AB A review with many refs. Recent theories on Alzheimers disease are opening new treatment lines, both pharmacol. as non-pharmacol. The conviction has already been reached that, in this ***neurodegenerative*** illness, it is necessary to plan a global treatment, with all sorts of measures for the patient, including the care-givers, and in which doctors and other sanitary professionals, as well as other social and economic agents, must take part. The aims of these treatments must be considered for every step in the clin. development of each patient given them the highest possible degree of self-sufficiency. Between new drugs being introduced we must emphasize "cholinergic drugs" (ranging from muscarinic agonists to aceticholinesterase inhibitors), "growth factors" (NGF, gangliosides, ***neurotrophins*** and glial factors), nootropics (similar in action to the former), and "aging factor neutralizers" (regulators of intraneuronal calcium and neutralizers or scavengers of free radicals). The anticholinesterasic tacrin has shown many secondary effects, due to its hepatotoxicity, but it is hoped that soon, new generation, less

toxic drugs will appear. There are some coadjutant drugs which can be employed, and others useful in the control of psychotic and depressive symptoms.

Even though we cannot yet talk of effective and attainable treatments at this moment, but we can hope that new drug ***administration*** routes and pharmacol. approaches (brain injections, slow drug diffusion pumps, ***neuron*** and glial ***cell*** implants, and gene ***therapy***) will, in the near future, be able to control the evolution of the illness.

=> s l4 and neuro?/ab,bi
227772 NEURO?/AB
301028 NEURO?/BI
L8 277 L4 AND NEURO?/AB,BI
=> d 1-10 bib ab
L8 ANSWER 1 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999577006 CAPLUS
TI Embryonic or stem-like cell lines produced by cross-species nuclear transplantation
IN Rob, James, Cibelli, Jose, Stice, Steven L.
PA University of Massachusetts, A Public Institution of Higher Education of the USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN CNT 1
PATENT NO. DATE

PL WO 9945100 A1 19990910 WO 1999-0910
19990302
W. AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SI, TJ, TM, MD, RU, TI, TM
RW, GH, GM, KE, LS, MW, SD, SI, SZ, UG, ZW, AT, BE,
CH, CY, DE, DK,

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG,

CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-32945 19980302

AB An improved method of nuclear transfer involving the transplantaion of differentiated donor cell nuclei into enucleated oocytes of a species different from the donor cell is provided. The resultant nuclear transfer units are useful for the prodn. of isogenic embryonic stem cells, in particular human isogenic embryonic or stem cells. These embryonic or stem-like cells are useful for producing desired differentiated cells and for introduction, removal or modification, of desired genes, e.g., at specific sites of the genome of such cells by homologous recombination.

These cells, which may contain a heterologous gene, are esp. useful in ***cell*** transplantation ***therapies*** and for *in vitro* study of cell differentiation. Also, methods for improving nuclear transfer efficiency by genetically altering donor cells to inhibit apoptosis, select for a specific cell cycle and/or enhance embryonic growth and development are provided.

L8 ANSWER 2 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999-569434 CAPLUS

TI Antioxidant activity and biologic properties of a procyanidin-rich extract from pine (*Pinus maritima*) bark, pycnogenol

AU Packer, L; Rimbach, G.; Virgili, F.
CS Department of Molecular and Cell Biology, University of California,
Berkeley, CA, USA

SO Free Radical Biol Med (1999), 27(5/6), 704-724

CODEN: FRBMED; ISSN: 0891-5849

FB Elsevier Science Inc.

DT Journal

LA English

AB There is growing interest in the biol. activities of plant exts. such as that obtained from the bark of the French maritime pine *Pinus maritima*. Pycnogenol (PYC) is a standardized ext. composed of flavonoids, mainly procyanidins and phenolic acids. Studies indicate that PYC components are highly bioavailable. Uniquely PYC displays greater biol. effects as a mixt. than its purified components do individually indicating that the components interact synergistically.

PYC has been reported to have cardiovascular benefits, such as a vasorelaxant activity, angiotensin-converting enzyme (ACE) inhibiting activity, and the ability to enhance the microcirculation by increasing capillary permeability. Investigations of the ***cellular*** mechanisms of these ***therapeutic*** effects have demonstrated that PYC has strong free radical-scavenging activity against reactive oxygen and nitrogen species. The oligomeric components of PYC contribute significantly to the ESR free radical signal. PYC also participates in the cellular antioxidant network as indicated by its ability to regenerate the ascorbyl radical and to protect endogenous vitamin E and glutathione from oxidative stress. PYC modulates NO metab. in activated macrophages by quenching the NO radical and inhibiting both iNOS mRNA expression and iNOS activity. The spectrum of different effects of NO in the circulation and the nervous system suggest the potential applications of PYC in immune and circulatory disorders as well as in ***neurodegenerative*** disease. PYC can bind to proteins, altering their structure and thereby modulating the activity of key enzymes and proteins involved in metabolic pathways. PYC effects redox-sensitive signal transduction pathways and alters gene expression. Aspects of PYC's activity are presented and discussed together with possible future implications and directions in the field of flavonoid research.

L8 ANSWER 3 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999-566152 CAPLUS

DN 131:167378

TI Derivation of cells and tissues from embryonic pre-stem ***cells*** for transplantation ***therapies***

IN Hodgen, Gary D.

PA Medical College of Hampton Roads, USA

SO PCT Int. Appl., 13 pp.

CODEN: PIXQD2

DT Patent

LA English

FAN,CNT 1
PATENT NO. -----
KIND DATE -----
APPLICATION NO. -----
DATE -----

PI WO 9443286 A2 19990902 WO 1999-US3897
19990224
W. AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM
RW, GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH,
CY, DE, DK, ES,
CG, CL, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-28395 19980224
AB Methods of treating a human patient having a disease, disorder or condition of the central nervous system are disclosed. The methods include obtaining a bone marrow sample from a human donor, isolating stromal cells from the bone marrow sample, and administering the isolated stromal cells to the central nervous system of the human patient, wherein the presence of the isolated stromal cells in the brain effects treatment of the disease, disorder or condition. Stromal cells which are isolated may be cultured *in vitro*, they may be genetically engineered to produce therapeutic compds., and/or they may be pre-differentiated prior to

AB A novel method of isolating and propagating a line of embryonic stem cells that originates from either morulae (pre-embryo) or blastocyst (ICM stem cells) is disclosed for the purpose of transplanting cells, tissues or organs.

L8 ANSWER 4 OF 277 CAPLUS COPYRIGHT 1999 ACS

AN 1999-563879 CAPLUS

TI Isolated stromal cells for use in the treatment of diseases of the central nervous system

IN Prokopp, Darwin J.; Stokes, David G.; Azizi, S. Autism; Phinney, Donald G.
PA MCP Hahnemann University, USA
SO PCT Int. Appl., 138 pp.
CODEN: PIXQD2
DT Patent
LA English
FAN,CNT 1
PATENT NO. -----
KIND DATE -----
APPLICATION NO. -----
DATE -----

PI WO 9443286 A2 19990902 WO 1999-US3897
19990224
W. AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN, MW, MX, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM
RW, GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH,
CY, DE, DK, ES,
CG, CL, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-28395 19980224
AB Methods of treating a human patient having a disease, disorder or condition of the central nervous system are disclosed. The methods include obtaining a bone marrow sample from a human donor,

isolating

stromal cells from the bone marrow sample, and administering the isolated stromal cells to the central nervous system of the human patient, wherein the presence of the isolated stromal cells in the brain effects treatment of the disease, disorder or condition. Stromal cells which are isolated may be cultured *in vitro*, they may be genetically engineered to produce therapeutic compds., and/or they may be pre-differentiated prior to

PI WO 9443286 A1 19990902 WO 1999-US4188
19990226

W. AU, CA, JP, NO

RW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT,
LU, MC, NL

PT, SE

PRAI US 1998-PV76273 19980227

administration into the central nervous system.

- L8 ANSWER 5 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999-500334 CAPLUS
TI New prospects for human stem-cell***cell*** therapy***
in the nervous system
AU Svendsen, Clive N.; Smith, Austin G.
CS MRC Cambridge Centre for Brain Repair, University of Cambridge, CB2 2PY, UK
SO Trends Neurosci. (1999), 22(8), 357-364
CODEN: TNSCDR; ISSN: 0166-2236
PB Elsevier Science Ltd.
- DT Journal
LA English
AB There are pluripotent stem cells in the adult brain that might not be very different from those found in bone marrow. Recent and profound advances in the field of ***neurogenesis***, which often rely on insights from studies of hematopoiesis and in some instances use cross-paradigms with this field, have already revealed that bone marrow has much in common with so-called 'brain marrow'. Proliferative progenitors and developmentally regulated mols. are hallmarks of both ***neurogenesis*** and hematopoiesis. This article will focus on recent advances in ***neurogenesis*** within a central core of the mature brain referred to as brain marrow, discussing its pluripotency and proliferative capacity, in vitro and mol. assays used in its study, and markers of ***neurogenic*** stem/progenitor cells. As hematopoiesis research has led to the discovery of numerous morphogenetic factors, it is anticipated that studies of ***neurogenesis*** should also uncover many new factors and genes that affect the growth and differentiation of neural cells. Recent breakthroughs in the stem-cell field prompt an inclusion of rationale for the persistence of normal stem/progenitor cells even in the aged brain. By analogy with hematopoiesis research, a thorough investigation of brain marrow should provide basic insights into developmental and persistent ***neurogenesis*** while anticipating ***Cell ***-transplant and gene ***therapies*** for debilitating ***neurol*** diseases.
- L8 ANSWER 6 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999-500330 CAPLUS
TI Marrow-mindedness: a perspective on ***neurogenesis***
and neural stem-cell technologies, and the strategies used to isolate and expand defined cell populations.
AU Scheffler, Bjorn; Horn, Meyer; Blumcke, Ingmar; Laywell, Eric D.; Coomes, Debra; Kuklev, Valery G.; Steinleiter, Dennis A.
CS Dept of Anatomy and Neurobiology, University of Tennessee, Memphis, TN, 38163, USA
SO Trends Neurosci. (1999), 22(8), 348-357
CODEN: TNSCDR; ISSN: 0166-2236
PB Elsevier Science Ltd.
- DT Journal
LA English
AB It would be of enormous benefit if human neural tissue could be generated in vitro as this would allow screening for ***neuroactive*** and provide a source of tissue for testing ***cellular*** and gene ***therapies*** for CNS disorders. It is now well established that pluripotent embryonic stem cells (ES cells) from the mouse can be propagated in culture and differentiated into a range of tissues, including ***neuronal*** and glial cells. In other studies, more-restricted neural stem cells have been isolated from both the developing and adult rodent brain. Current reports now describe similar pluripotent and neural stem cells cultured from human embryos. While the exact nature of these cells continues to be explored, they can be grown for extended periods of time while retaining the capacity for ***neuronal*** and glial differentiation. In some cases, they have been shown to integrate into the developing or damaged adult brain. This article reviews their bio!, with a focus on the possible links between ES-cell and neural stem-cell technologies, and the strategies used to isolate and expand defined cell populations.
- L8 ANSWER 7 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999-483394 CAPLUS
TI Methods of treatment using MAO-A and MAO-B inhibitors such as L-depronyl
IN Thomas, Thomas N.
PA USA
SO PCT Int. Appl. 42 pp.
CODEN: PIXD2
DT Patent
LA English
FAN CNT 1
PATENT NO. KIND DATE APPLICATION NO.
DATE
- PI US 5929041 A 19990727 US 1996-710219 19960913
US 5837681 A 19981117 US 1996-506176 19960223
WO 9730722 A1 19970828 WO 1997-US2677
19970214
- W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, IP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TI, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW, GH, GM, KE, LS, MV, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BI, CF, CG, CL, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAUS 1998-PV7718 19980127
AB Effects of MAO-A or MAO-B inhibitors such as L-depronyl on both cerebral and peripheral vasculature, on nonvascular smooth muscle, on the nervous system, and on platelets, RBC, WBC, mast cells, macrophages, and glial cells are disclosed. The effects are the result of a mode of action for MAO-A or MAO-B inhibitors such as L-depronyl which is totally unrelated to selective inhibition of MAO-A and/or MAO-B. Therapeutic methods of using MAO-A or MAO-B inhibitors such as L-depronyl to treat a variety of disorders are disclosed.
- ***neurotrophin***
factor (GDNF) protein product
IN Magen, Ella
PA Amgen Inc., USA
SO U.S., 24 pp. Cont.-in-part of U. S. 5,837,681.
CODEN: USXXCAM
DT Patent
LA English
FAN CNT 2
PATENT NO. KIND DATE APPLICATION NO.
DATE
- PI US 5929041 A 19990727 US 1996-710219 19960913
US 5837681 A 19981117 US 1996-506176 19960223
WO 9730722 A1 19970828 WO 1997-US2677
19970214
- W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, PB, Elsevier Science Ltd.

- KZ, LC,
NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TI, TM, TR, TT, UA, UG, UZ,
VN, AM,
AZ, BY, KG, KZ, MD, RU, TI, TM
RW, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI,
FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML,
MR, NE, SN, TD, TG
CA 2217565 AA 19970828 CA 1997-2217565 19970214
AU 9722779 A1 19970910 AU 1997-22779 19970214
AU 691443 B2 19980514
EP 822829 A1 19980211 EP 1997-906022 19970214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
MC, PT,
IE, SI, LT, LV, FI, RO
CN 1181704 A 19980513 CN 1997-190100 19970214
JP 11504351 T2 19990420 JP 1997-530323 19970214
NO 9704767 A 19971222 NO 1997-4767 19971015
US 1996-606176 19960223
US 1996-710219 19960913
WO 1997-102677 19970214
- AB The present invention relates generally to methods for preventing and/or treating injury or degeneration of cochlear (and vestibular) hair cells and spiral ganglion ***neurons*** by administering glial cell line-derived ***neurotrophic*** factor (GDNF). The invention relates more specifically to methods for treating sensorineural hearing loss in vestibular disorders. Thus, at 8 days after treatment of 4 guinea pigs with cisplatin the loss of hair cells in the middle turn of the cochlea was 34, 47, 42, and 41%, resp.; whereas, after injection of GDNF (1 mg/ml.) into the right middle ear, the hair cell loss was reduced to 16, 23, 21, and 29%, resp.
- L8 ANSWER 9 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999-464356 CAPLUS
TI Feline immunodeficiency virus gene therapy vectors
IN Johnston, Julie C.; Sauter, Sybille L.; Hau, David; Sheridan, Philip Lee;
Hardy, Stephen F.; Dubensky, Thomas W.; Yee, Jing-Kuan
PA Chiron Corporation, USA
SO PCT Int Appl, 170 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN,CNT 1
PATENT NO. KIND DATE APPLICATION NO.
DATE

- serum-free defined medium congt basic fibroblast growth factor (bFGF), leukemia inhibitory factor (LIF), and epidermal growth factor (EGF). Using these three factors, the cell cultures expand and remain multipotent for at least 1 yr in vitro. This period of expansion results in a 107-fold increase of this heterogeneous population of cells. Upon differentiation, they form ***neurons***, astrocytes, and oligodendrocytes, the three main phenotypes in the CNS. Moreover, GABA-immunoreactive and tyrosine hydroxylase-immunoreactive ***neurons*** can be identified. These results demonstrate the feasibility of long-term in vitro expansion of human neural progenitor cells. The advantages of such a population of neural precursors for allogeneic transplantation include the ability to provide an expandable, well-characterized, defined cell source which can form specific ***neuronal*** or glial subtypes. (c) 1999 Academic Press.
=> s 12 and neuro7/ab.bi
227772 NEURO7/AB
301028 NEURO7/AB.BI
L9 485 L2 AND NEURO7/AB.BI
=> s 19 and 11
L10 66 L9 AND L1
=> d 1-10 bib ab
- L8 ANSWER 10 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1998-452-02 CAPLUS
TI In Vitro Expansion of a Multipotent Population of Human Neural Progenitor Cells
AU Carpenter, Melissa K.; Cui, Xia; Hu, Zhongyi; Jackson, Jennifer; Sherman, Sandy; Seiger, ANG.k.e; Wahlberg, Lars U.
CS Cell and Molecular Neurobiology, CytoTherapeutics, Inc., Lincoln, RI,
02865, USA
SO Exp. Neurol. (1999), 158(2), 265-278
CODEN: EXNEAC; ISSN: 0014-4886
PB Academic Press
DT Journal
LA English
AB The isolation and expansion of human neural progenitor cells have important potential clin. applications, because these cells may be used as graft material in ***cell*** ***therapies*** to regenerate tissue and/or function in patients with central nervous system (CNS) disorders. This paper describes a continuously dividing multipotent population of progenitor cells in the human embryonic forebrain that can be propagated in vitro. These cells can be maintained and expanded using a
- L10 ANSWER 1 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998-432617 CAPLUS
TI Identification of neural stem ***cells*** and its application to the ***therapeutics*** of damaged brains
AU Kawaguchi, Ayano; Okano, Hideyuki
CS Biomed. Res. Cent., Osaka Univ. Grad. Sch. Med., Japan
SO Saishin Igaku (1999), 54(7), 1721-1729
CODEN: SAIGAK; ISSN: 0370-8241
PB Saishin Igakusha
DT Journal: ***General Review***
LA Japanese
AB A review, with 22 refs, on ***neuronal*** development in fetal stage of mammals, establishment of selective culture of neural stem cell,
- PI WO 9936511 A2 19990722 WO 1999-US1194
19990119
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LY, MD, MG,
MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TI,
TM, TR,
TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW, GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH,
CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BI, CF,
CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-71731 19980116
US 1998-86825 19980526
US 1999-114955 19990104
US 1999-231235 19990115
AB Disclosed are gene therapy vectors based upon the feline immunodeficiency virus, as well as related packaging cell lines, methods for prodn., and methods of use.

study on its differentiation regulation, existence of neural stem cell in adults, and possibility of clin. application of neural stem cells.

L10 ANSWER 2 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:299361 CAPLUS

DN 131:128230

TI ***Neuroendocrine*** differentiation in prostatic carcinoma
AU Abrahamsson, Per-Anders
CS Department of Urology, University Hospitals of Malmö and Lund, University of Lund, Lund, S-221 85, Swed.

SO Prostate (N.Y.) (1999), 39(2), 133-148

PB Wiley-Liss, Inc.

DT Journal; ***General Review***

LA English

AB A review, with 159 refs. Information is presented on prostatic differentiation ***neuroendocrine*** cells and ***neuroendocrine*** in prostatic carcinoma. The prognostic and therapeutic implications of ***neuroendocrine*** differentiation in prostatic carcinoma are reviewed. Data are presented that support the intriguing link between ***neuroendocrine*** differentiation, tumor progression, and androgen-independent prostate cancer. The hormones, and the receptors, expressed by prostatic ***neuroendocrine*** cells are investigated in order to elucidate their significance for prognosis and therapy. The prognostic significance of ***neuroendocrine*** differentiation in prostatic malignancy has been controversial, but recent studies employing markers such as chromogranin A and ***neuron***-specific enolase suggest that ***neuroendocrine*** differentiation, as reflected by increased tissue expression and/or blood levels of these ***neuroendocrine*** secretory products, correlates with poor prognosis, tumor progression, and androgen-independence. Since all malignant ***neuroendocrine*** cells are devoid of androgen receptors and since ***neuroendocrine*** phenotypic expression is not suppressed by androgen ablation, clonal propagation of androgen receptor-neg.

neuroendocrine cells may play an important role in the pathway towards the androgen-independent state of prostatic carcinoma. This would have significant implications for the treatment of prostate cancer, as several of the hormones known to be expressed by ***neuroendocrine***-differentiated, malignant prostatic ***cells*** are potential

candidates for drug ***therapy***. A limited no. of hormones have been tested in this context, in particular somatostatin, bornesin, and serotonin. ***Neuroendocrine*** differentiation in carcinoma of the prostate appears to be assocd. with poor prognosis, tumor progression, and the androgen-independent state, for which there is currently no therapy. Therefore, new therapeutic protocols and trials need to be developed to test drugs based on ***neuroendocrine*** hormones and/or their antagonists. An evaluation of this new therapeutic approach against prostatic carcinoma with ***neuroendocrine*** differentiation, including hormone-refractory cancer, is easily justified, since these tumors are unresponsive to current modes of therapy.

L10 ANSWER 3 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:237724 CAPLUS
DN 131:39041

TI The therapeutic potential of CXC chemokine blockade in acute inflammation in the brain
AU Anthony, Daniel C.; Walker, Katherine; Perry, V. Hugh
CS CNS Inflammation Group, Centre for Neuroscience at Southampton, University of Southampton, SO16 7PX, UK
SO Expert Opin. Invest. Drugs (1999), 8(4), 363-371
CODEN: ECOLDR, ISSN: 1354-3784
PB Ashley Publications
DT Journal; ***General Review***
LA English
AB A review with 63 refs. Mammalian ***neurons*** of the central nervous system (CNS) are terminally differentiated, and there is little endogenous capacity of the CNS to repair itself. Peripheral tissue injury, disease or infection results in a stereotypical inflammatory response to protect the host from pathogens and to promote tissue repair. However, collateral or "bystander" damage is characteristic of any inflammatory response. Thus, it is apparent that the CNS has evolved mechanisms to regulate tightly the acute inflammatory response, and in particular to restrict the recruitment of neutrophils, in an attempt to protect itself from the potentially damaging consequences of inflammation in the brain. However, neutrophils are not always excluded from the brain. Indeed, they are found in large nos. in the brain parenchyma following traumatic lesions,

stroke lesions, and in rodents, during the "window of susceptibility".

Therapy targeted at blocking excitotoxic ***cell*** death has not successfully transferred from rodent models of stroke to human stroke patients. Restricting leukocyte entry to the brain, thereby inhibiting the inflammatory response, may prove to be a more practical therapeutic approach. The evidence presented in this review suggests that antagonizing the effects of CXC chemokines may represent one route to achieve this goal.

L10 ANSWER 4 OF 66 CAPLUS COPYRIGHT 1999 ACS

AN 1999:169142 CAPLUS

TI Apoptosis: molecular mechanisms

AU Solary, Eric

CS Unité INSERM 517, Mort cellulaire et cancer, Groupe Biologique et Thérapeutique des Cancers (JE515), Facultés de Médecine et de Pharmacie, Dijon, 21033, Fr.

SO C. R. Séances Soc. Biol. Ses Fil. (1998), 192(6), 1065-1076
CODEN: CRSBAW, ISSN: 0037-9026

PB SGS

DT Journal; ***General Review***

LA French
AB A review with 35 refs. Apoptosis is a genetically programmed cell death that is required for morphogenesis during embryogenic development and for tissue homeostasis in adult organisms. In most cases, apoptosis involves cytochrome c release from mitochondria. In the cytosol, cytochrome c combines with APAF-1 in the presence of ATP to activate caspase-9; that, in turn, activates effector caspases such as caspase-3. Bcl-2 and related proteins control cytochrome c release from the mitochondria whereas IAP (for inhibitor of Apoptosis) mols. modulate the activity of caspases. Plasma membrane receptors such as Fas (CD95, APO-1), characterized by a so-called "death domain" in their cytoplasmic domain, can activate the caspase cascade through adaptor mols. such as FADD (Fas-Associated protein with a Death Domain). Dysregulation of the apoptotic machinery plays a role in the pathogenesis of various diseases, and mols. involved in ***cell*** death pathways are potential ***therapeutic*** targets in immunol., ***neurol***, cancer, infectious and inflammatory diseases.

- L10 ANSWER 5 OF 66 CAPLUS COPYRIGHT 1999 ACS
 AN 1999:55994 CAPLUS
 DN 130:265542
 TI Cellular and molecular basis of estrogen's
 neuroprotection :
 potential relevance for Alzheimer's disease
 AU Inestrosa, Nibaldo C.; Marzollo, Maria-Paz; Bonnefont, Andrea
 B.
 CODEN: MONBEW; ISSN: 0893-7648
 CS Departamento de Biología Celular y Molecular, Facultad de
 Ciencias, Pontificia Universidad Católica de Chile, Chile
 SO Mol. Neurobiol. (1998), 17(1-3), 73-86
 PB Humana Press Inc.
 DT Journal; ***General Review***.
 LA English
 AB A review, with 124 refs. Alzheimer's disease (AD) is one of the
 most common types of dementia among the aged population, with a
 higher prevalence in women. The reason for this latter observation
 remained unsolved for years, but recent studies have provided evidence that a
 lack of circulating estrogen in postmenopausal women could be a
 relevant factor. Moreover, follow-up studies among postmenopausal
 women who had received estrogen-replacement therapy (ERT), suggested that they
 had a markedly reduced risk of developing AD. In addn., studies among
 older women who already had AD indeed confirmed that a decrease in
 estrogen levels was likely to be an important factor in triggering the
 pathogenesis of the disease. In this review article, the authors will discuss the
 evidence suggesting that estrogen may have a protective role
 against AD, mainly through its action as: a trophic factor for cholinergic
 neurons, a modulator for the expression of apolipoprotein E (ApoE)
 in the brain, an antioxidant compd. decreasing the
 neuronal damage caused by oxidative stress, and a promoter of the physiol.
 nonenzymologic processing of the amyloid precursor protein
 (APP), decreasing the prodn. of the amyloid-beta-peptide (A.**beta.**), a key
 factor in the pathogenesis of AD

L10 ANSWER 6 OF 66 CAPLUS COPYRIGHT 1999 ACS
 AN 1999:52452 CAPLUS
 DN 130:280326
 TI Pathological immunoreactions of glial cells in Alzheimer's disease
 and possible sites of interference

AU Schubert, P.; Ogata, T.; Miyazaki, H.; Marchini, C.; Ferroni, S.;
 Rudolph, K.
 CS Department of Neuromorphology, Max Planck Institute for
 Neurobiology,
 Martinsried, Austria
 SO J. Neural Transm., Suppl. (1998), 54(Alzheimer's Disease: From
 Basic Research to Clinical Applications), 167-174
 CODEN: INTSD4; ISSN: 0303-6995
 PB Springer-Verlag Wien
 DT Journal; ***General Review***.
 LA English
 AB A review with 29 refs. A significant role of a pathol. glial cell
 activation in the pathogenesis of Alzheimer's disease is supported
 by the growing evidence that inflammatory proteins, which are produced
 by reactive astrocytes, promote the transformation of diffuse
 beta-amyloid deposits into the filamentous, ***neurotoxic*** form. A no. of
 vicious circles, driven by the release of TNF-alpha and free
 oxygen radicals from microglial cells, may cause an upregulated microglial
 activation and their prodn. of interleukin-1 which triggers,
 secondarily, the crucial activation of astrocytes. Reactive functional changes of
 glial cells seem to be controlled by an altered balance of the second
 messengers Ca2+ and cAMP and can be counterregulated by the
 endogenous cell modulator adenosine which strengthens the cAMP-dependent
 signaling chain. A further reinforcement of the homeostatic adenosine
 effects on glial cells by drugs, such as propranolol, may add to
 neuroprotection in Alzheimer's disease.

L10 ANSWER 7 OF 66 CAPLUS COPYRIGHT 1999 ACS
 AN 1999:39754 CAPLUS
 DN 130:261279
 TI Peripheral ***neuroopathy*** with nucleoside antiretrovirals:
 factors, incidence and management
 AU Moyle, Graeme J.; Sadler, Martin
 CS Kobliter Clinic, Chelesea and Westminster Hospital, London, UK
 SO Drug Saf. (1998) 19(6), 481-494
 CODEN: DRSAEA; ISSN: 0114-5916
 PB Adis International Ltd.
 DT Journal; ***General Review***.
 LA English
 AB A review with 67 refs. Distal sym. peripheral
 neuroopathy is a common adverse experience in persons with HIV infection. This
 condition, which presents as a pain, numbness, burning and/or dysesthesia
 initially in the feet, is often multi-factorial in its origin. Nucleoside analog
 reverse transcriptase inhibitors represent an important contributor to
 the behavioral symptoms or the assoc'd. neural degeneration. In recent

L10 ANSWER 8 OF 66 CAPLUS COPYRIGHT 1999 ACS
 AN 1999:20180 CAPLUS
 DN 130:205199
 TI Cellular delivery of ***neurotrophic*** factors as a potential
 treatment for Huntington's disease
 AU Einerich, Dwaine; Kordover, Jeffrey H.; Isackson, Ole
 CS Department of Neuroscience, Alkermes, Inc., Cambridge, MA,
 USA
 SO CNS Regener. (1999), 477-502. Editor(s): Tuszynski, Mark H.;
 Kordover,
 Jeffrey H. Publisher: Academic, San Diego, Calif.
 CODEN: 67C3A3
 DT Conference; ***General Review***.
 LA English
 AB A review with approx. 100 refs. Huntington's Disease (HD) is a
 devastating
 neurodegenerative disorder with no effective treatments
 for the

years, the advent of appropriate animal models has permitted the evaluation of multiple therapeutic strategies. One of the more promising approaches currently under preclin. investigation and clin. consideration is the use of ***neurotrophic*** factors that might slow the progression or even prevent the onset of the behavioral and pathol. consequences of HD. This chapter highlights the use of transplanted genetically modified cells as a means of delivering ***neurotrophic*** factors. Studies in both rodent and nonhuman primate models of HD suggest that trophic factors such as NGF and CNTF exert marked ***neuroprotective*** effects upon the vulnerable striatal ***neurons*** that degenerate in HD.

Although the mechanisms by which these factors exert their beneficial effects remain unclear, their clear cut potency in both rodent and primate models of HD provide the hope that a means of preventing or slowing the relentlessly progressive motor and cognitive declines in HD may be forthcoming. Furthermore, excitotoxicity has been implicated in a variety of pathol. conditions including ischemia, and ***neurodegenerative*** diseases such as Huntington's, Parkinson's, and Alzheimer's. Accordingly, delivered ***neurotrophic*** factors may provide one means of preventing the cell loss and assoc. behavioral abnormalities of these and possibly other human disorders.

L10 ANSWER 9 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:20171 CAPLUS
DN 130:245945
TI Neural stem cell lines for CNS repair
AU Martinez-Serrano, Alberto; Snyder, Evan Y.
CS Center of Molecular Biology "Severo Ochoa," Autonomous University of Madrid-CSIC, Madrid, Spain
SO CNS Regener. (1999), 203:250. Editor(s): Tuszyński, Mark H.; Kordower, Jeffrey H. Publisher: Academic, San Diego, Calif.
CODEN: 67CYA3
DT Conference: ***General Review***
LA English
AB A review with 112 refs. The establishment and use of stable, engratifiable, multipotent neural stem cell lines have recently added an exciting

new dimension to strategies for cell replacement and gene transfer

to the diseased mammalian CNS. These neural stem cell clones can serve as convenient, well-controlled models for the in vivo study of CNS development and regeneration; can constitute readily available, well-characterized, safe sources of graft material for the replacement of multiple types of degenerated neural cells; and can provide excellent vehicles for the transfer of genes encoding diffusible and non-diffusible factors directly to the CNS. By exploiting their basic biol. properties, these cells are able to bypass restrictions imposed by the blood-brain barrier to deliver therapeutic gene products in a sustained, direct, and perhaps regulated fashion throughout the CNS (either because they intrinsically produce these substances or because they have been genetically engineered ex vivo to do so). Furthermore, although they may disseminate these gene products throughout the brain, they nevertheless restrict that distribution to only the CNS. In addn., they may replace dysfunctional neural cells in both a site-specific and more global manner (circumventing the concern that in many alternative gene transfer techniques "new" genetic information is supplied to "old" neural circuits, many of which may have degenerated). Neural stem cell clones may be used for ***neurodegenerative*** conditions that occur both during development and in the mature brain. In fact, they appear to be capable of altering their migration and differentiation in response to certain as yet unspecified signals elaborated during active ***neurogenesis***.

Thus, these vehicles may overcome many of the limitations of viral and non-neuronal cellular vectors, as well as pharmacol. and genetic interventions. A growing body of evidence has, indeed, affirmed the efficacy of a neural stem cell-based strategy for the replacement of defective or absent genes and cells, and has suggested that re-population of the diseased or injured CNS with such cells may promote both anatomical and behavioral recovery in animal models of ***neurodegenerative*** conditions. These recent exps. with clones of rodent neural progenitor cells in vitro and in vivo as well as their possible use for ***cell*** replacement and gene ***therapy***.

=> d 11-20 bib ab

human origin.

L10 ANSWER 10 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:20170 CAPLUS
DN 130:245944
TI The use of neural progenitor ***cells*** for ***therapy*** in the CNS disorders
AU Ray, Jasodhar; Palmer, Theo D.; Shihabuddin, Lanya S.; Gage, Fred H.
CS Laboratory of Genetics, Salk Institute, La Jolla, CA, USA
SO CNS Regener. (1999), 183:201. Editor(s): Tuszyński, Mark H.; Kordower, Jeffrey H. Publisher: Academic, San Diego, Calif.
CODEN: 67CYA3
DT Conference: ***General Review***
LA English
AB A review with 84 refs. In recent years a significant no. of ***neurot*** diseases have been defined at the mol. level.
Somatic gene ***therapy*** using genetically modified non-***neuronal*** ***cells*** expressing ***therapeutic*** factors have been successfully used in animal models of ***neurodegenerative*** diseases. Ability to grow central nervous system (CNS)-derived neural progenitor cells has proven to be extremely useful to study a diverse phenomenon including the fate choice, differentiation, and synaptic maturation of cells. Immortal or perpetual cultures of neural progenitor cells implanted into the rodent brain survive, migrate, and integrate in the host cytoarchitecture. These cells can be genetically modified to express therapeutic gene products. The ability of the implanted cells to integrate in the host brain and express transgene products *in situ* offer potential approaches for gene therapy in certain CNS diseases. The utility of this approach has already been explored in animal models of ***neurodegenerative*** diseases. This chapter reviews the recent advances made in understanding the nature and potentiality of neural progenitor cells in vitro and in vivo as well as their possible use for ***cell*** replacement and gene ***therapy***.

L10 ANSWER 11 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:17041 CAPLUS
DN 130:177630

- T1 A commentary on glial cell line-derived ***neurotrophic*** factor (GDNF): from a glial secreted molecule to gene therapy
AU Bohn, Martha C.
CS Childrens Memorial Institute for Education and Research, Northwest University Medical School, Chicago, IL, 60614, USA
SO Biochem Pharmacol (1998), 57(2), 135-142
CODEN: BCPA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal; ***General Review***
LA English
AB A review with 72 refs. Glial cell line-derived ***neurotrophic*** factor (GDNF) was identified as a consequence of the hypothesis that glia secrete factors that influence growth and differentiation of specific classes of ***neurons***. Glia are a likely source of adult, ***neurotrophic*** factors; however, this strategy has not been applied. The discovery of GDNF in 1993 led to an abundance of studies that within only a few years qualified GDNF as a bona fide ***neurotrophic*** factor. Of particular interest are studies demonstrating the effectiveness of GDNF protein in ameliorating ***neurodegeneration*** in animal models of Parkinson's disease and amyotrophic lateral sclerosis (ALS). It remains to be determined whether GDNF will be an effective therapy in humans with these diseases. However, since these diseases are slowly progressive and the CNS relatively inaccessible, the delivery of GDNF as a therapeutic mol. to the CNS in a chronic manner is problematic. Studies addressing this problem are applying viral vector mediated transfer of the GDNF gene to the CNS in order to deliver biosynthesized GDNF to a specific location in a chronic manner. Recent studies suggest that these GDNF gene therapy approaches are effective in rat models of Parkinson's disease. These studies are reviewed in the context of what developments will be needed in order to apply GDNF gene therapy to the clinic.
- L10 ANSWER 12 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:802182 CAPLUS
DN 130:207923
TI Calcium and cellular death
AU Sattler, Rita; Tymianski, Michael
CS Playfair Neuroscience Unit, The Toronto Hospital Research Institute, Toronto, ON, Can.
SO Integ Aspects Calcium Signalling (1998), 267-290 Editor(s): Verkhratsky, Alexej Nestorovich; Toescu, Emil C. Publisher: Plenum, New York, N. Y.
CODEN: 67AWAL
DT Conference; ***General Review***
LA English
AB A review, with many refs. Recent years have seen significant advances in our conceptualization of mechanisms by which Ca2+ ions may mediate cell death. In spite of the complexities assocd. with ***neuronal*** Ca2+ homeostasis, it appears that ***neurons*** possess a powerful machinery for dealing with Ca2+ excess. Thus, 'Ca2+ excess', conceptualized as an unusually large cellular Ca2+ load, is in itself insufficient to cause ***neurotoxicity***. Instead, the relationship between Ca2+ influx and ***neurotoxicity*** is significantly

- DT Journal; ***General Review***
LA Japanese
AB A review with 85 refs. Apoptosis of retinal ganglion cells has been observed in glaucomatous models and human glaucomatous eyes in expl. pathol. studies. It seems that retinal ganglion cells in glaucomatous optic ***neuropathy*** die by a process similar to programmed cell death. Deprivation of ***neurotrophic*** factors, ischemia, chronic elevation of glutamate, and disorganized NO metab. are suspected to be factors, affecting ***neuronal*** loss in glaucoma, and most of these factors are known to activate the mechanism of cellular suicidal death. One of the common switches for the death mechanism seems to be in the mitochondria and to be controlled by Bcl-2 family proteins. A major goal of ***neuronal*** cell death research in glaucomatous ***neuropathy*** is to identify its mol. components and mechanisms of regulation. This information will lead to ***therapeutic*** agents that can modulate the ***cell*** death process in the treatment of glaucomatous ***neuropathy***.
- L10 ANSWER 13 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:802182 CAPLUS
DN 130:207923
TI Calcium and cellular death
AU Sattler, Rita; Tymianski, Michael
CS Playfair Neuroscience Unit, The Toronto Hospital Research Institute, Toronto, ON, Can.
SO Integ Aspects Calcium Signalling (1998), 267-290 Editor(s): Verkhratsky, Alexej Nestorovich; Toescu, Emil C. Publisher: Plenum, New York, N. Y.
CODEN: 67AWAL
DT Conference; ***General Review***
LA English
AB A review, with many refs. Recent years have seen significant advances in our conceptualization of mechanisms by which Ca2+ ions may mediate cell death. In spite of the complexities assocd. with ***neuronal*** Ca2+ homeostasis, it appears that ***neurons*** possess a powerful machinery for dealing with Ca2+ excess. Thus, 'Ca2+ excess', conceptualized as an unusually large cellular Ca2+ load, is in itself insufficient to cause ***neurotoxicity***. Instead, the relationship between Ca2+ influx and ***neurotoxicity*** is significantly more complex, as it depends not only on the quantity of Ca2+ which enters the cell, but also on the subcellular compartments to which Ca2+ ions gain access. This feature of Ca2+ ***neurotoxicity*** can be measured both using total Ca2+ flux measurements with radiolabeled Ca2+ ions, or using fluorescent free Ca2+ indicators. However, Ca2+ ion fluxes must be meticulously restricted to distinct influx pathways for the dependence of Ca2+ ***neurotoxicity*** on a given subcellular location of Ca2+ ions to be reliably inferred. The corollary of these recent observations is that " ***neurotoxic*** " Ca2+ ions must trigger specific intracellular signaling cascades for ***neurotoxicity*** to occur, since such cascades do not appear to be triggered when Ca2+ ions enter cells through "non toxic" pathways. Thus, the mol. substrates governing toxic pathways must also be compartmentalized with toxic Ca2+ fluxes. In many ***neurons***, toxic Ca2+ entry occurs through NMDA receptors which are implicated in numerous physiol. functions. Therefore, it is likely that mol. substrates which participate in toxic phenomena also subserve physiol. roles under less stressful conditions. This raises the likelihood that, rather than being caused by a non-specific disruption of the cell's homeostatic machinery, Ca2+ ***neurotoxicity*** is a pathol. extension of physiol. Ca2+ signaling. Thus, future research must be aimed at revealing the specific signal transduction pathways involved in Ca2+ ***neurotoxicity***, and at identifying mol. targets whose pharmacol. or genetic manipulation might produce improved ***therapies*** for Ca-mediated ***cell*** death.
- L10 ANSWER 14 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:798523 CAPLUS
DN 130:148113
TI Telomeres and telomerase: targets for cancer chemotherapy?
AU Perry, Philip J.; Kelland, Lloyd R.
CS Cancer Research Campaign Biomolecular Structure Unit and Centre for Cancer Therapeutics, The Institute of Cancer Research, Surrey, SM2 5NG, UK
SO Expert Opin. Ther. Pat. (1998) 8(12), 1567-1586
CODEN: EOTPBC; ISSN: 1344-3776
PB Ashley Publications
DT Journal; ***General Review***
LA English

- AB A review with 141 refs. Telomerase is a specialised ribonucleoprotein comprising, at present, 3 known components: the human telomerase RNA component (hTR); the human telomerase reverse transcriptase catalytic subunit (hTERT), and TP1, a telomerase-assocd. protein.

Applications involving telomerase have been proposed in the fields of engineering, diagnostics/prognostics and ***therapeutics***. In the diagnostics area, around 85% of human cancers have been shown to possess telomerase activity, while such activity is not detectable in most somatic cells. In some cases (notably ***neuroblastomas***, gastric and breast tumors), higher levels of telomerase activity were assocd. with poor prognosis. Telomerase activity, which has generally been measured using a highly sensitive PCR-based TRAP assay, may also be assessed to monitor residual disease following surgery and/or chemotherapy. As telomerase appears to be selectively expressed in tumors vs. normal cells, many have proposed that the enzyme represents a good target for inhibition. Efforts are underway to target various components of the telomerase/telomere machinery including the hTR template region using antisense oligonucleotides and peptide nucleic acids (PNAs), some of which inhibit at the nanomolar level, hTERT, and the telomere/telomerase interaction. Small-mol. inhibitors of telomerase have recently been described. These include a series of regiosomeric dianiodanthracene-9,10-diones (the best of which inhibit telomerase in cell-free assays with IC50 values of 1 - 5 .mu.M) and porphyrin-based mols. These mols. have been proposed to act via stabilization of guanine-quadruplexes, structures assoc. with telomeres and telomerase. Reverse transcriptase inhibitors, such as AZT triphosphate, have also been shown to inhibit telomerase. This will clearly be an area where, in the near future, potent inhibitors will be developed thus permitting further target validation expts. to be performed in tumor-bearing mice and ultimately in cancer patients.

DN 130:191-238

TI Approaches in treating nerve cell death with calcium chelators comprising, at present, 3 known components: the human telomerase RNA component (hTR); the human telomerase reverse transcriptase catalytic subunit (hTERT), and TP1, a telomerase-assocd. protein.

SO Cell Death Dis. Nerv. Syst. (1999), 609-631. Editor(s): Koliatsos, Vassilis E.; Ratan, Rajiv R. Publisher: Humana, Totowa, N. J. CODEN: 67ARA6 DT Conference; ***General Review*** LA English

AB A review, with 137 refs., discussing current knowledge on the role of Ca2+ buffers as probes of mechanisms leading to nerve ***cell*** death and ***therapeutic*** agent for Ca2+-dependent ***neurotoxicity***.

DN 130:16 OF 66 CAPLUS COPYRIGHT 1999 ACS AN 1998:787842 CAPLUS

TI Trophic factors as therapeutic agents for diseases characterized by ***neuronal*** death

AU Koliatsos, Vassilis E.; Mochetti, Italo CS Departments of Pathology (Neuropathology), Neurology, Neuroscience, and Psychiatry and Behavioral Science, The Johns Hopkins University School of Medicine, Baltimore, MD, USA SO Cell Death Dis. Nerv. Syst. (1999), 545-591. Editor(s): Koliatsos, Vassilis E.; Ratan, Rajiv R. Publisher: Humana, Totowa, N. J. CODEN: 67ARA6 DT Conference; ***General Review*** LA English

AB A review with 305 refs. with the following key sections: trophic factors ***therapies*** ; ***neuronal*** ***cell*** as biol. ***therapeutic*** target (distal and proximal interventions); ***neurobiol*** . of trophic factors (basic tenets); clin. potential of trophic peptides; novel concepts in the ***neurobiol*** of trophic factors; activity-related changes in trophic factor expression and utilization; challenges in the clin. pharmacol. of trophic factors, and conclusions.

DN 130:90-109 CAPLUS

TI Retinal regeneration mechanism and application towards congenital retinal diseases therapy

AU Tomita, Hiroshi; Abe, Toshiaki; Tamoi, Makoto CS Medical School, Tohoku University, Japan

SO Rinsho Kagaku (Osaka) (1998), 24(9), 1276-1282 CODEN: RIKAER; ISSN: 0355-0323

PB Esato K. K. DT Journal; ***General Review*** LA Japanese

AB A review with 13 refs., on history of retina regeneration, retinal pigment epithelial cell differentiation in retina regeneration; retina regeneration from neural precursor cells; mol. mechanism of retina regeneration; and therapy of congenital retinal diseases by ***neuroretina*** regeneration; Gene ***therapy*** , retina ***cell*** transplant, and ***neurotrophic*** and growth factors.

DN 130:5820-59341 CAPLUS

TI Gemcitabine and paclitaxel combinations in non-small-cell lung cancer

AU Dombernowsky, Per; Giaccone, Giuseppe; Sandler, Alan; Schwartzenau, Gilberto CS Department of Oncology Herlev Hospital, Herlev, DK 2730, Den. SO Semin. Oncol. (1998), 25(4, Suppl. 9), 44-50 CODEN: SOLGAV; ISSN: 0093-7754

PB W. B. Saunders Co. DT Journal; ***General Review*** LA English

AB A review with 44 refs. Gemcitabine and paclitaxel are new cytotoxic agents that have been used both as single agents and in combination, particularly with cisplatin, in the ***therapy*** of non-small- cell lung cancer (NSCLC) with promising results. The lack of overlapping toxicities and different mechanisms of action of gemcitabine and paclitaxel make the combination of these drugs appealing in the treatment of NSCLC. A no. of phase I and II trials are evaluating the use of this combination of cytotoxic agents as 1st-line therapy and as 2nd-line therapy in patients with advanced NSCLC. In ongoing phase II trials using a 21-day schedule, the combination of gemcitabine and paclitaxel therapy appears to be well-tolerated, with response rates ranging 29%-58% and hematol. toxicities that are mild to moderate in severity. Other reported toxicities included alopecia, fatigue, and flu-like symptoms, which were also mild to moderate. However, grade 2/3 ***neurotoxicity*** was also reported. In conclusion, preliminary results from these early phase II trials of gemcitabine/paclitaxel combination therapy in advanced NSCLC

DN 130:90544 CAPLUS

TI Retinal regeneration mechanism and application towards congenital retinal diseases therapy

AU Tomita, Hiroshi; Abe, Toshiaki; Tamoi, Makoto CS Medical School, Tohoku University, Japan

SO LIO ANSWER 15 OF 66 CAPLUS COPYRIGHT 1999 ACS AN 1998:787844 CAPLUS

feasibility and clinical efficacy of convective drug delivery for treatment of a ***neurological*** disorder, the investigators selectively ablated globus pallidus internus (GPI) ***neurons*** with quinolinic acid (QA), an excitotoxin, in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced model of primate parkinsonism. METHODS: After the parameters of convective distribution to the GPI were confirmed by infusion of biotinylated albumin into the GPI of a primate (Macaca mulatta), seven adult monkeys of this species were rendered either fully parkinsonian by intravenous injections of MPTP (five animals) or hemiparkinsonian by a right-sided intracarotid injection of this agent (two monkeys). Using convection-enhanced delivery to the GPI, animals were infused with either QA (three fully parkinsonian, two hemiparkinsonian) or saline (two fully parkinsonian). The three fully parkinsonian animals that underwent GPI lesioning with QA had substantial improvement of PD symptoms, manifested by a marked increase in activity ($34 \pm 2\%$; mean \pm standard deviation) and dramatic improvement of parkinsonian clinical scores. In contrast, the control animals did not improve (activity monitor change = $-1.5 \pm 0.5\%$). The two hemiparkinsonian animals that underwent QA lesioning of the GPI had dramatic recovery of extremity use. Histological examination revealed selective neural ablation of GPI ***neurons*** (mean loss 8.7%) with sparing of surrounding gray and white matter structures. No animal developed worsening signs of PD or ***neurological*** deficits after infusion. CONCLUSIONS: Convection-enhanced delivery of QA permits selective, region-specific (GPI), and safe lesioning of ***neuronal*** subpopulations, resulting in dramatic improvement in parkinsonian symptomatology. The properties of convection-enhanced delivery indicate that this method could be used for ***neurosurgery*** for medically refractory PD and that it may be ideal for ***cell***-specific ***therapeutic*** ablation or trophic treatment of other targeted structures associated with CNS disorders.

L12 ANSWER 2 OF 28 MEDLINE
AN 1999242345 MEDLINE
DN 99242345 MEDLINE

T1 Leukocytapheresis therapy by extracorporeal circulation using a leukocyte removal filter [editorial].
AU Suenaga J; Yoshida M; Yamawaki N; Yamashita Y
SO Ther Apher. (1998 Feb) 2 (1) 31-6. Ref: 12
Journal code: DBB. ISSN: 1091-6660.
CY United States
DT Editorial
General Review, (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199907
EW 19990703
AB Leukocytapheresis therapy has been used to try to treat such intractable diseases as autoimmune and ***neurologic*** diseases, achieving good results. However, a number of ***problems*** have been identified in leukocyte removal by thoracic duct drainage or continuous centrifugal separation; namely the high risk, expensive cost, and complicated operation. Asahi Medical Co. has developed an innovative solution for such conventional ***problems***. Its new leukocyte removal filter (Cellsorba) is capable of removing white blood cells by perfusion of whole blood by means of simple extracorporeal circulation. Leukocytapheresis ***therapy*** using the ***Cellsorba*** column is being confirmed as extremely effective for many inflammatory diseases, as well as in autoimmune and ***neurologic*** diseases. This paper outlines information about the Cellsorba column and introduces several reports on therapeutic results.

L12 ANSWER 3 OF 28 MEDLINE
AN 1999094700 MEDLINE
DN 99094700 MEDLINE

T1 Distal symmetrical peripheral ***neuropathy*** is a common adverse experience in persons with HIV infection. This condition, which presents as a pain, numbness, burning and/or dysesthesia initially in the feet, is often multi-factorial in its origin. Nucleoside analogue reverse transcriptase inhibitors represent an important contributor to peripheral ***neuropathy***. Specifically, around 10% of patients receiving stavudine or zalcitabine and 1 to 2% of didanosine recipients may have to discontinue therapy with these agents due to ***neuropathy***. Prompt withdrawal of these therapies enables gradual resolution of signs and symptoms in most patients, although a period of symptom intensification may occur shortly after withdrawal. Risk factors for developing peripheral ***neuropathy*** during nucleoside analogue ***therapy*** include low CD4+ ***cell*** count (<100 cells/mm³), a prior history of an AIDS defining illness or neoplasm, a history of peripheral ***neuropathy***, use of other ***neurotoxic*** agents including high alcohol (ethanol) consumption and nutritional deficiencies such as low serum hydroxocobalamin levels. Thus, patients at increased risk of peripheral ***neuropathy*** should potentially avoid the use of the ***neurotoxic*** nucleoside analogues or be more carefully monitored during therapy. Management of this ***problem*** includes patient education, prompt withdrawal of the likely causative agent (giving consideration not to leave the patient on a sub-optimal therapy regimen) and simple analgesia, with augmentation with tricyclic antidepressants or anticonvulsant agents when pain is severe. New agents that may assist in managing this condition include levacercarnine (acetyl-L-carnitine)

AB Distal symmetrical peripheral ***neuropathy*** is a common adverse experience in persons with HIV infection. This condition, which presents as a pain, numbness, burning and/or dysesthesia initially in the feet, is often multi-factorial in its origin. Nucleoside analogue reverse transcriptase inhibitors represent an important contributor to peripheral ***neuropathy***. Specifically, around 10% of patients receiving stavudine or zalcitabine and 1 to 2% of didanosine recipients may have to discontinue therapy with these agents due to ***neuropathy***. Prompt withdrawal of these therapies enables gradual resolution of signs and symptoms in most patients, although a period of symptom intensification may occur shortly after withdrawal. Risk factors for developing peripheral ***neuropathy*** during nucleoside analogue ***therapy*** include low CD4+ ***cell*** count (<100 cells/mm³), a prior history of an AIDS defining illness or neoplasm, a history of peripheral ***neuropathy***, use of other ***neurotoxic*** agents including high alcohol (ethanol) consumption and nutritional deficiencies such as low serum hydroxocobalamin levels. Thus, patients at increased risk of peripheral ***neuropathy*** should potentially avoid the use of the ***neurotoxic*** nucleoside analogues or be more carefully monitored during therapy. Management of this ***problem*** includes patient education, prompt withdrawal of the likely causative agent (giving consideration not to leave the patient on a sub-optimal therapy regimen) and simple analgesia, with augmentation with tricyclic antidepressants or anticonvulsant agents when pain is severe. New agents that may assist in managing this condition include levacercarnine (acetyl-L-carnitine)

L12 ANSWER 4 OF 28 MEDLINE
AN 1999081926 MEDLINE
DN 99081926 MEDLINE

T1 Use of gene marking technologies in oncology
AU Bremner M
CS Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, Texas 77030, USA.

SO FORUM, (1998 Oct-Dec) 8 (4) 342-53. Ref: 67
Journal code: COR. ISSN: 1121-8142.
CY Italy
DT Journal Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
EM 199904
EW 19990401
AB Investigation of the mechanism of relapse in patients receiving stem ***cell*** rescue as ***therapy*** for malignant disease has been facilitated by gene marking studies. These studies have shown the marker gene to be present in malignant cells in the patient at the time of relapse, indicating that infused stem cells can contribute to disease recurrence. As normal progenitor cells are also marked and can be tracked in vivo, these studies have also helped us learn how haemopoietic stem cells respond to manipulation, for example with growth factors. Second generation studies with multiple, modified vectors are beginning to provide information about a wider variety of clinical and biological issues, including the efficacy of purging. Although marker studies have been useful for haematological malignancy and for ***neuroblastoma***, they are hampered by the low efficiency of marking achieved by retroviral vectors. For many malignancies, marking efficiencies are insufficient for useful information to be obtained. This ***problem*** may be overcome by the introduction of vectors that, unlike retroviruses, can stably integrate in cells that are not in cycle at the time of vector exposure. Other improvements will focus on the marker genes themselves, using marker elements that are simpler to track and will not produce any modification of the cells' behaviour. Finally, marker studies have proved safe so far, but follow-up of the treated patients continues.

L12 ANSWER 5 OF 28 MEDLINE
AN 1999051537 MEDLINE
DN 99051537
TI Promoting remyelination as a future therapeutic principle in multiple sclerosis? Remyelinisierungsförderung als zukünftiges Therapieprinzip der Multiplen Sklerose?
AU Pohlau D; Aktas O; Epplen C; Hartung H-P; Hoffmann V;
Prantek H
CS Neurologische Klinik, Ruhr-Universität Bochum am St. Josef
Hospital.
SO NERVENARZT, (1998 Oct) 69 (10) 841-50. Ref: 12
Journal code: NWS. ISSN: 0028-2804.
CY GERMANY. Germany. Federal Republic of
DT Journal Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
EM 199904
EW 19990402
AB Multiple sclerosis (MS), the most common ***neurological*** autoimmune disorder diagnosed in young adults, is characterised by the repeated occurrence of demyelinating lesions within the central nervous system (CNS). Promotion of remyelination in the brain and spinal cord constitutes a potential strategy for therapeutic intervention in MS and other demyelinating diseases. Three different principles are known to promote remyelination in the CNS of different animal models. Application of growth factors, transplantation of myelin-forming ***cells*** and intravenous immunoglobulin (IVIg) ***therapy***. However, the systemic application of growth factors could be limited by effects on unaffected tissue. For successful transplantation we still have the ***problem*** of homologous cells not tolerated by a immunological different organism. Currently the required combination of growth factors needed to cultivate human homologous cells is not known, so that cells suitable for transplantation are still not available. Nevertheless, there is increasing evidence for beneficial effects of IVIg therapy on the promotion of remyelination in humans. In this review we summarise recent findings on the regulation of myelin sheath development and oligodendrocyte differentiation, and discuss the presented strategies in the context of possible clinical application for the therapy of MS.

DT Journal Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
EW 19990204
AB Metachromatic leukodystrophy (MLD) is a lysosomal storage disease, caused by deficiency of arylsulfatase A (ASA), that manifests primarily in the white matter of the nervous system. Currently, no specific treatment exists that will reverse its fatal outcome. Replacement therapy has been hampered by the blood-brain barrier (BBB). To circumvent this ***problem*** we designed an ex vivo gene therapy strategy that includes the retrovirus-mediated ASA transduction of cells, such as activated lymphocytes, that are able to traverse the BBB or other membranes of the CNS. For this purpose, two recombinant retroviruses based on the pLXSN vector were produced, containing the wild-type ASA cDNA or a pseudodeficiency ASA cDNA, which encodes a smaller enzyme with normal activity. After transduction, ASA activity increased more than 100-fold in fibroblasts from an MLD patient. Furthermore, ASA-transduced MLD PBLS expressed 30 times higher ASA activity when compared with control PBLS. Moreover, cell culture experiments demonstrated that transduced fibroblasts could efficiently transfer ASA to deficient cells across a transwell barrier, whereas transduced MLD lymphocytes could transfer ASA to deficient fibroblasts only by direct cell-to-cell contact. Finally, ASA was taken up by normal oligodendrocytes and Schwann cells, the target myelinating glial ***cells*** for ***therapy*** in MLD. These data suggest possible short-term strategies for transfer of ASA into the CNS via transduced autologous cells while long-term strategies, related to autologous transduced bone marrow transplant, take effect in patients.

L12 ANSWER 7 OF 28 MEDLINE
AN 1998043387 MEDLINE
DN 98043387
TI Lack of immune responses to immediate or delayed implanted allogeneic and xenogenic Schwann cell suspensions.
AU Herrmann S; Wunderlich G; Rosenbaum C; Hanemann C O;
Muler H W; Stichel C
C Molecular Neurobiology Laboratory, Department of Neurology,
CS United States

Dusseldorf,
Germany
SO GLIA, (1997 Nov) 21 (3) 299-314.
Journal code: GLI. ISSN: 0894-1491.
CY United States
DT Journal; Article, (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 19980204
EW 19980204
AB Previous studies have shown that Schwann ***cell***
implantation offers a potential ***therapeutic*** approach to a variety of
neurodegenerative disorders and traumatic injuries. In a
clinically relevant paradigm, however, the implantation of
autologous Schwann cells is ***problematic*** and the use of
heterogenetic Schwann cells will be required. In the present study we addressed
this important issue and analysed the immunogenicity and survival of
allogeneic and xenogeneic Schwann cell suspension grafts in a prelesioned
CNS fiber tract, the transected postcommisural fornix of the adult Wistar rat.
Cultured Schwann cells from Wistar rat or human peripheral nerve were
injected either immediately or after a delay into the transection site
and the spatio-temporal pattern of leukocyte infiltration and of major
histocompatibility antigen expression was characterized and
semiquantitatively with immunocytochemical methods. Our main findings are that (1)
invasive cerebral lesions induce the expression of MHC class I and II
antigens, but only sparse infiltration of T-lymphocytes, (2) both allogeneic and
xenogeneic discordant Schwann cell suspension grafts, from either
neonatal or adult peripheral nerve, survive without any overt signs of
rejection for up to 10 weeks after implantation, and (3) delayed implantation
procedures have no effect on immune responses to allogeneic
Schwann cell grafts. These results demonstrate that there is no marked ongoing
immune reactions to heterogeneic Schwann cell suspension grafts and that
long-term survival of cross-species Schwann cell grafts can be
achieved in the absence of any immunosuppressive treatment. Thus the
conditions for functional transplantation of Schwann cells across immunological
barriers seem to be favourable and will have implications for future
cross-species studies, and possibly also for clinical application.

112 ANSWER 8 OF 28 MEDLINE
DN 97472951 MEDLINE
TI The use of nonneuronal cells for gene delivery.
AU Snyder E Y, Senut M C
CS Department of Neurology, Harvard Medical School, Children's
Hospital, Boston, Massachusetts 02115, USA
SO NEUROBIOLOGY OF DISEASE, (1997) 4 (2) 69-102. Ref:
222
CY United States
DT Journal; Article, (JOURNAL ARTICLE)
General Review, (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199801
EW 19980104
AB The implantation of genetically engineered nonneuronal cells can provide an effective method for achieving localized delivery of discrete molecules to the CNS or for providing substrates for regrowth of neural structures. Most primary nonneuronal cells have the advantage of being easily obtainable from the prospective host for ex vivo retrovirus-mediated genetic manipulation (most will be mitotic in culture) and reimplantation as an autologous graft (circumventing the ***problem*** of immune rejection). As primary cells, they are unlikely to be tumorigenic. The most vexing ***problem*** for such systems remains the apparent loss of transgene expression from viral promoters after prolonged periods of engraftment. Much effort is currently being directed at optimizing sustained transgene expression by varying the promoters, by varying the cell types to be engineered, or by regulating expression by enhancing promoter function or substrate availability. While nonneuronal cells are excellent vehicles for achieving passive delivery of substances to the CNS, they lack the ability to incorporate into the host cyoarchitecture in a functional manner (e.g., make synaptic contacts). For this reason, not only may certain essential circuits not be re-formed, but the regulated release of certain substances through feedback loops may be missing. While apparently unimportant for some substances (e.g., ACh), for others (e.g., NGF), their unregulated, inappropriate, excessive, or

ectopic release may actually be detrimental to the host. Furthermore, the loss of foreign gene expression (the bane of gene ***therapy***) may leave engineered nonneuronal ***cells*** incapacitated, whereas tissue originating from brain may intrinsically produce various CNS factors allowing correction to proceed despite inactivation of the introduced gene. In fact, CNS-derived tissue may provide as-yet-unrecognized endogenous neural-specific substances which are equally as beneficial to the host as the gene in question. Thus, future developments in gene delivery to the brain for some conditions may emphasize using ***neurons*** or neural progenitors for ex vivo manipulations (Fisher, 1997) and refining techniques for the direct injection of therapeutic genes into ***neurons*** in vivo (see Snyder and Fisher, 1996). For a wide variety of conditions, however, using nonneuronal cellular vehicles or even nonbiologic synthetic vehicles may be efficient, effective, and safe strategies for the passive delivery of therapeutic molecules to discrete regions of the CNS. In fact, this approach may come closer than any other to immediate human applications.

112 ANSWER 9 OF 28 MEDLINE
AN 97246615 MEDLINE
DN 97246615
TI Cellular and molecular ***neurosurgery*** : pathways from concept to reality--part I: target disorders and concept approaches to gene therapy of the central nervous system.
AU Zlokovic B V, Apuzzo M L
CS Department of Neurological Surgery, Childrens Hospital Los Angeles, University of Southern California School of Medicine, USA.
SO NEUROSURGERY, (1997 Apr) 40 (4) 789-803; discussion 803-4. Ref: 99
Journal code: NZL. ISSN: 0148-396X
CY United States
DT Journal; Article, (JOURNAL ARTICLE)
General Review, (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199709
EW 19970901
AB Recent advances in cellular and molecular biology and better understanding of genetic and biochemical bases of different central nervous system (CNS) disorders have made gene therapy of the CNS a realistic goal. Concept
approaches for gene therapy of CNS disorders are reviewed and

include the following: 1) gene replacement with a single normal allele to correct the inherited global ***neurodegenerative*** disorders, such as enzyme deficiencies; 2) brain repair to restore the function of a particular subset of cells that were lost because of a ***neurodegenerative*** process; 3) gene therapy of brain tumors; and 4) gene therapy of stroke.

Techniques of viral vector-mediated CNS transfer of a ***therapeutic*** gene, transplantation of genetically modified ***cells***, fetal embryonic implantation and/or implantation of genetically engineered neural progenitor cells, and production of a specific enzyme, ***neurotransmitter***, and/or growth factor are discussed with respect to the therapeutic potential for global and localized CNS ***neurodegenerative*** disorders and stroke. Transfection of the CNS tumor cells with the drug susceptibility ("suicide") gene and/or "toxic" gene and antisense strategies and a concept of adoptive immunotherapy of brain tumors are also discussed. Other approaches, such as transfer of drug-resistant genes and monoclonal antibody gene transfer, are briefly discussed. In addition to summarizing current principles of gene therapy for several groups of CNS disorders, the issues that remain to be resolved in clinical reality, such as delivery of the genetic material and regulation of the cellular expression of the transgene, and the negatives associated with the concept of gene therapy, such as transient gene expression, toxicity of viral proteins, drawbacks of antisense therapy, and the ***problem*** of immune response to the transfected protein, have been also identified.

SO CLINICAL NEUROSCIENCE, (1995-96) 3 (5) 317-21. Ref. 42
 Journal code: B9U ISSN: 1065-6766.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 199705
 EW 19970503
 AB The discovery of major ***neurodegenerative*** mechanisms has opened the way to the development of novel therapeutic approaches. Gene therapy now enables researchers to overcome certain ***problems*** inherent to pharmacotherapy and to the grafting of embryonic cells. The production of recombinant adenoviruses are promising for *in vivo* gene therapy involving ***neuroprotective*** (Ad-SOD), ***neurotrophic*** (Ad-NGF) as well as restorative (Ad-TF) strategies. In addition, human neural progenitors offer great potential as vehicles for *ex vivo* gene ***therapy*** to replace degenerated ***cells*** in advanced stages of ***neurodegenerative*** diseases. This paper describes the clinical values of the new generations of adenoviral vectors.

L12 ANSWER 11 OF 28 MEDLINE
 AN 9639809 MEDLINE
 DN 9639809
 TI [***Cell*** transplantation and gene ***therapy*** in Parkinson disease].
 Celltransplantation och genterapi vid Parkinsons sjukdom.
 AU Björklund A
 CS Wallenberg Neurocentrum, Institutionen för Fysiologi och Neurovetenskap,
 Lunds Universitet.
 SO NORDISK MEDICIN, (1996 Sep) 111 (7) 225-9.
 Journal code: O4K. ISSN: 0029-1420.
 CY Sweden
 DT Journal; Article; (JOURNAL ARTICLE)
 LA Swedish
 EM 199701
 EW 19970104
 AB In 1995 the Anders Järne Prize for medical research was shared by Professor Lars Olson, Stockholm (Nord Med 1/96), and Professor Anders Björklund, Lund. Using newly developed methods, Anders Björklund has mapped important parts of the central nervous system and ***neurotransmitters*** in the brain. Björklund and co-workers Cervi, Paris, France.

have therapeutically transplanted ***neurones*** to parts of the brain that, owing to disease or injury, are deficient in essential ***neurotransmitters***. During recent years, the transplantation of fetal nerve cells has been introduced as a possible new therapeutic procedure in Parkinson's disease. Although promising results have been obtained in clinical trials both in Europe and North America, the technique needs further improvement to enhance cell survival, effectiveness and reproducibility. Moreover, an essential long-term goal is to eliminate dependence on a continuous supply of fetal tissue, which is both ethically and practically ***problematic***. Current research is focused on ways to promote the survival and growth of grafted cells, and on the use of gene transfer procedures to generate alternative dopamine-producing of trophic factor-producing cells.

L12 ANSWER 12 OF 28 MEDLINE
 AN 96227618 MEDLINE
 DN 96227618
 TI [Insulin producing ***cells*** as ***therapy*** in diabetes mellitus].
 Insulinsezierende Zellen zur Therapie des Diabetes mellitus.
 AU Schmed JW; Hohmann HE; Neuward C B
 CS Medizinische Universitätsklinik, Karl Franzens Universität, Graz
 SO NATURWISSENSCHAFTEN, (1996 Jan) 83 (1) 1-5. Ref. 41
 Journal code: NSW. ISSN: 0028-1042.
 CY GERMANY; Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA German
 FS Priority Journals
 EM 199609
 AB Even with intensive insulin therapy it is impossible to reach physiological blood glucose levels in insulin-dependent diabetes mellitus. Because of the high costs and technical ***problems*** involved in islet ***cell*** transplantation broad applicability of this ***therapy*** seems uncertain. An alternative approach is the development of molecular-engineered insulin-producing clonal cell lines.

The main interest is in rodent insulinoma cell lines and ***neuroendocrine*** AT-20ins cells. This paper reviews the current knowledge about glucose-stimulated insulin secretion and the ***problems*** that have to be solved before these ***cells*** can be used for ***therapy*** in diabetes mellitus.

L12 ANSWER 13 OF 28 MEDLINE
 AN 96124619 MEDLINE

DN 96124619
TI Gaucher disease.
AU Ohashi T
CS Jikei University School of Medicine, Department of Pediatrics.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1995 Dec) 53 (12) 2943-6. Ref: 12
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Japanese
EM 199605
AB Gaucher disease is an inherited metabolic disease characterized by deficient activity of lysosomal enzyme, known as a glucocerebrosidase.
Three clinical phenotype were documented depends on the onset of disease and ***neuronal*** involvement. Deficient activity of glucocerebrosidase results in progressive accumulation of glucocerebroside mainly in bone marrow derived macrophages. Diagnosis was made based on enzymatic activity in various tissue including WBC and fibroblasts. Molecular diagnosis was also possible. However, it is difficult to differentiate the three phenotypes. Although bone marrow transplantation and enzyme infusion therapy are both effective, the inherent ***problems*** limits their application. Gene therapy based on transfer of the ***therapeutic*** gene to hematopoietic stem ***cells*** were started in this year in USA.

L12 ANSWER 14 OF 28 MEDLINE
AN 96121848
DN 96121848
TI Transplantation of microencapsulated hepatocytes for liver function replacement.
AU Dixit V, Gittnick G
CS UCLA School of Medicine, Department of Medicine
90024-7019, USA.
SO JOURNAL OF BIOMATERIALS SCIENCE, POLYMER EDITION, (1995) 7 (4) 343-57.
Journal code: AY7. ISSN: 0920-5063.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199603
AB Recent advances in cell biology and biotechnology have led the way for a greater understanding of ***cell*** function and the potential ***therapeutic*** use of transplanted ***cells*** for

treating a wide array of illnesses. Treatment of disease by transplantation of normal healthy cells, for the replacement of specific biological deficiencies or as a form of auxiliary support for a failing organ, offers important therapeutic applications and also serves as a model for assessing cellular physiology. In the long-term, cell transplantation may also have potential in the development of artificial organ support systems for sustaining patients with severe and chronic diseases such as diabetes, liver failure, endocrine and exocrine disorders, ***neurological*** abnormalities, and congenital metabolic defects. Several groups have demonstrated the feasibility and efficacy of cell transplantation in providing specific function in various experimental animal models of human disease. However, without adequate immunosuppression, complications due to tissue rejection remain a significant ***problem***. Microencapsulation of cells within a synthetic semipermeable membrane, prior to transplantation, has been proposed for circumventing immunological complications following transplantation. The microcapsule's semipermeable membrane allows permeant molecules to freely diffuse across while preventing the microencapsulated cells from escaping. This membrane also keeps unwanted substances, such as cells and antibodies, from entering the microcapsule. Thus, microencapsulation provides an innovative and unique technique for the transplantation of foreign tissue and cells without the need for immunosuppression.

L12 ANSWER 15 OF 28 MEDLINE
AN 96005511
DN 96005511
TI A phase II trial of melbarone (NSC 336628) as salvage ***therapy*** for squamous ***cells*** carcinoma of the cervix. A Gynecologic Oncology Group Study.
AU Look K Y, Blessing J A, Williams L; Morris M
CS Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, USA..
NC CA 27469 (NCI)
CA 37517 (NCI)
SO AMERICAN JOURNAL OF CLINICAL ONCOLOGY, (1995 Mar) 6 (2) Oct 18 (5) 441-3.
CY United States
EM 199603
AB Recent advances in cell biology and biotechnology have led the way for a greater understanding of ***cell*** function and the potential ***therapeutic*** use of transplanted ***cells*** for

DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals, Cancer Journals
EM 199601
AB Twenty-seven patients with previously irradiated unresectable recurrent squamous carcinoma of the cervix who had failed one prior cytotoxic regimen received 1,000 mg/m² per day of melbarone given by continuous i.v. infusion for 5 days every 4 weeks through a central line. One patient was never treated, and four were inevaluable for response, leaving 26 patients evaluable for toxicity and 22 evaluable for response. The major adverse effect was myelosuppression with 6/26 (23%) experiencing ***neutropenia***. This ***neurotoxicity*** may have been secondary to iatrogenic hyponatremia caused by the large volumes of 5% glucose infusion required at the original infuse concentration. After the concentration of the melbarone infuse was increased to 4 mg/m², no further ***problems*** with hypotension, ***neurotoxicity*** were encountered. The overall response rate was 2/22 (9.0%) (95% confidence interval 1.1-29.2%). In this pretreated population with recurrent squamous cervical carcinoma, melbarone exhibited only minimal activity.

L12 ANSWER 16 OF 28 MEDLINE
AN 94281278
DN 94281278
TI Recent advances in diagnosis and treatment of small cell non-small cell lung cancer.
AU Sorensen J B; Hansen H H
CS Department of Oncology, National University Hospital/Rigshospitalet, Copenhagen, Denmark..
SO CURRENT OPINION IN ONCOLOGY, (1994 Mar) 6 (2) 162-70. Ref: 63
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English
FS Priority Journals

NM

Despite much effort and many published reports, progress in diagnosing and treating lung cancer has been slow. The use of monoclonal antibodies for detection of metastasis and * **neuroendocrine*** markers for subclassification of non-small cell lung cancer into different prognostic groups may be useful in future staging and treatment.

Dose-intensive chemotherapy in small cell lung cancer is still experimental, which is also the case for prophylactic cranial irradiation. Adjuvant chemotherapy for completely resected patients with non-small cell lung cancer may be associated with a marginal survival benefit, which also seems to hold true for patients with advanced disease when compared with untreated control subjects solely receiving supportive care. The modest survival benefit is achieved at the cost of increased toxicity. Neoadjuvant treatment remains a controversial issue, one of the major ***problems*** being the lack of an effective standard systemic ***therapy*** in non-small * **cell*** lung cancer.

L12 ANSWER 17 OF 28 MEDLINE
AN 94116614 MEDLINE
DN 94116614
TI A model three-dimensional culture system for mammalian dopaminergic precursor cells: application for functional intracerebral transplantation.AU Spector D H; Boss B D; Strecke R E
CS Department of Psychiatry and Behavioral Science, SUNY at Stony Brook
LA English
FS Priority JournalsSO EXPERIMENTAL NEUROLOGY, (1993 Dec) 124 (2):253-64.
Journal code: EQF. ISSN: 0014-4886.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199404

AB Grafts of fetal neural tissue, rich in dopamine (DA)

* **neurons***

have previously been shown to improve the symptoms of parkinsonism, both in humans and in animal models. In order to circumvent some of the ***problems*** associated with ***cell*** transplant

(DT Journal; Article; (JOURNAL ARTICLE))

General Review, (REVIEW)
(REVIEW, TUTORIAL)

LA English

FS Priority Journals; Cancer Journals

EM 199402

AB ***Neurodegenerative*** disorders such as Parkinson's, Alzheimer's, and Huntington's disease are becoming ever more prominent in our society.

A direct approach towards therapeutic treatment of these diseases is through replacement therapy where normal tissue is transplanted back to the nervous system. Recently, significant progress has been achieved with transplants in Parkinson's disease, but the process is heavily dependent

on an unstable and ***problematic*** source of fetal tissue. Neural stem cells may become the tissue/ ***cell*** source necessary for developing the ***therapeutic*** potential of neural transplantation.

Stem ***cells*** are self-renewing, multipotent and could provide a well-characterized and clean source of transplantable material. A number

of new in vitro approaches have led to the development of continuously propagated stem cells that are potential candidates for nervous system transplantation. These include oncogene-induced immortalization and growth-factor stimulation of naturally occurring central and peripheral nervous system stem cells. The nature of these cells and their suitability for transplantation into the CNS will be evaluated.

L12 ANSWER 19 OF 28 MEDLINE
AN 92146986 MEDLINE
DN 92146986
TI Integrative assessment of the developmental pharmacology and developmental toxicology, with special reference to the brain.AU Fujii T
CS Department of Pharmacology, Teikyo University School of Medicine, Tokyo, Japan..
SO NIPPON YAKURIGAKU ZASSHI, FOLIA PHARMACOLOGICA JAPONICA, (1991 Dec) 93 (6):419-34. Ref. 92
Journal code: F2X. ISSN: 0015-3691.

CY Japan

DT Journal; Article; (JOURNAL ARTICLE)
General Review, (REVIEW)
(REVIEW, TUTORIAL)

- LA Japanese
FS Priority Journals
EM 199205
- AB Increasing numbers of ***neurotoxins*** or ***therapeutic*** agents that have specific target. ***cells*** or receptors can be used to assess the developmental correlation between the structure and function of various organs including the brain. Patients with chronic diseases are now able to maintain their social activities but still must be medicated for a long period of their life. This might increase the potential hazard of prenatal drug exposure in the progeny. Functional teratology is quite a new concept in ***neuroscience***. Recent observations of our laboratory and those of others suggest that the sensitive period for functional teratology might encompass the whole stage of fetal life in animals and humans. The shortage of precise information on the developmental integration of the structure and function of the ***neurons*** with different properties is a ***problem*** to be solved for the further progress of developmental pharmacology and toxicology. Single exposures to drugs at a different stage during the gestational period of rats or mice might provide more useful information on the relationship between the lesioned area and related functional disorders manifested postnatally. This paper reviews recent advances in developmental ***neuropharmacology*** and functional ***neuroteratology*** including beneficial points of the short-term exposures to drugs.
- L12 ANSWER 20 OF 28 MEDLINE
AN 92117458 MEDLINE
DN 92117458
- TI [Rare tumor of the posterio-superior mediastinum. Therapeutic approach. Apropos of a case. Review of the literature].
- Tumeur rare du mediastin posterio-superieur. Attitude propos d'un cas. Revue de la litterature.
AU Zimmermann J M; De Graeve B; Cador L; Colonna M A;
Cohleance J F; Lemestie L
SO ANNALES DE CHIRURGIE, (1991) 45 (8) 695-8. Ref: 36
Journal code: SOE. ISSN: 0003-3944.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
- LA French
EM 199204
- ***neurotoxic*** effect. A double screening of suramin analogs on HT29-D4 and C6 cells allowed us to identify a new candidate antineoplastic drug. NFO36.
- L12 ANSWER 22 OF 28 MEDLINE
AN 91056694 MEDLINE
DN 91056694
- TI A case of long-term survival of patient with complicated diffuse metastatic leptomeningeal carcinomatosis secondary to lung adenocarcinoma.
AU Watanabe A; Mizobe M; Ogawa Y; Takei N; Nomoto H; Urata C; Mano K; Hohjo S; Iimamura T
CS Second Department of Internal Medicine, Teikyo University, School of Medicine, Tokyo, Japan.
SO NIHON KYOBU SHIKKAN GAKKAI ZASSHI. JAPANESE JOURNAL OF THORACIC DISEASES,
(1990 Aug) 28 (8) 1130-5.
Journal code: KQD. ISSN: 0301-1542
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
EM 199103
- AB A case of long-term survival of a female patient with complicated diffuse metastatic leptomeningeal carcinomatosis (PMLC) secondary to lung cancer is reported. A 36-year-old woman, hospitalized with a chief complaint of headache and unproductive cough, was diagnosed as having primary lung adenocarcinoma (T4N1M1 oss) and was given systemic chemotherapy. Although progressive deterioration of her headache continued, repeated ***neurological*** examination, cerebrospinal fluid (CSF) examination, and cranial CT scans failed to show evidence of metastasis to the central nervous system, and the only finding suggesting CNS involvement was an elevated CEA level in CSF. Later in the course of her treatment, the patient suddenly lost her vision and subsequently consciousness due to acute increased intracranial pressure, and emergency ventricular drainage was performed for ***therapeutic*** and diagnostic purposes.
- Malignant ***cells*** were found in CSF obtained from a ventricular drainage and she was treated successfully by systemic and intrathecal chemotherapeutic agents. She was discharged after a ventriculoperitoneal shunt operation

- AB The authors report an exceptional case of giant cell tumour of the third thoracic vertebra revealed by its mediastinal development. Despite intimate involvement of the large mediastinal vessels, a double surgical approach, starting with sternotomy to ensure vascular control then anterolateral thoracotomy, allowed curative resection of this tumor. Treatment was completed by a second ***neurosurgical*** operation followed by 5,000 rads of radiotherapy. Based on a review of the literature, the authors discuss the pathogenesis and consider the various ***therapeutic*** raised by giant cell***
problems
cell
tumours of the vertebrae (situated above the sacrum).
- L12 ANSWER 21 OF 28 MEDLINE
AN 92097077 MEDLINE
DN 92097077
- TI Double screening of suramin derivatives on human colon cancer cells and on neural ***cells*** provides new ***therapeutic*** agents with reduced toxicity.
AU Baghdigian S; Niekel P; Fantini J
CS INSERM U270 Faculty of Medicine, Marseille, France.
SO CANCER LETTERS, (1991 Dec 1) 60 (3) 213-9.
Journal code: CMX. ISSN: 0304-3835
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199204
- AB Suramin is a polyanionic compound currently used under evaluation for anticancer activity. One of the main ***problems*** encountered during clinical trials was an adverse ***neurotoxic*** effect, probably due to a direct cytotoxic effect on neural cells. Suramin is also known to trigger differentiation of human colon cancer cells, yet a chronic treatment induces a lysosomal storage disorder. The aim of this study was to evaluate suramin analogs for their effect: (i) on the lysosomal system of the human colon cancer cell clone HT29-D4, and (ii) on C6 glioma cell growth and morphology. One of the derivatives tested, NFO36, induced terminal differentiation of HT29-D4 cells without any impairment of the lysosomal system. Furthermore, in contrast to suramin, NFO36 did not alter C6 cell growth and morphology. We conclude that there is a relationship between the ability of a suramin derivative to induce a lysosomal storage disorder in human colon cancer cells and its

- ***neurotoxic*** effect. A double screening of suramin analogs on HT29-D4 and C6 cells allowed us to identify a new candidate antineoplastic drug. NFO36.
- L12 ANSWER 22 OF 28 MEDLINE
AN 91056694 MEDLINE
DN 91056694
- TI A case of long-term survival of patient with complicated diffuse metastatic leptomeningeal carcinomatosis secondary to lung adenocarcinoma.
AU Watanabe A; Mizobe M; Ogawa Y; Takei N; Nomoto H; Urata C; Mano K; Hohjo S; Iimamura T
CS Second Department of Internal Medicine, Teikyo University, School of Medicine, Tokyo, Japan.
SO NIHON KYOBU SHIKKAN GAKKAI ZASSHI. JAPANESE JOURNAL OF THORACIC DISEASES,
(1990 Aug) 28 (8) 1130-5.
Journal code: KQD. ISSN: 0301-1542
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
EM 199103
- AB A case of long-term survival of a female patient with complicated diffuse metastatic leptomeningeal carcinomatosis (PMLC) secondary to lung cancer is reported. A 36-year-old woman, hospitalized with a chief complaint of headache and unproductive cough, was diagnosed as having primary lung adenocarcinoma (T4N1M1 oss) and was given systemic chemotherapy. Although progressive deterioration of her headache continued, repeated ***neurological*** examination, cerebrospinal fluid (CSF) examination, and cranial CT scans failed to show evidence of metastasis to the central nervous system, and the only finding suggesting CNS involvement was an elevated CEA level in CSF. Later in the course of her treatment, the patient suddenly lost her vision and subsequently consciousness due to acute increased intracranial pressure, and emergency ventricular drainage was performed for ***therapeutic*** and diagnostic purposes.
- Malignant ***cells*** were found in CSF obtained from a ventricular drainage and she was treated successfully by systemic and intrathecal chemotherapeutic agents. She was discharged after a ventriculoperitoneal shunt operation

for hydrocephalus; a double-dome reservoir was used for continuous intrathecal administration of the anticancer drugs, and a shunt filter was located in the tube to prevent the dissemination of cancer cells. In addition to methotrexate and cytosine arabinoside, ACNU and interleukin-2 were administered intrathecally without serious adverse effects, but no apparent therapeutic effects were noted either. She survived over 2 years after DMLC was first diagnosed. At autopsy DMLC secondary to lung adenocarcinoma was confirmed, but no evidence of leucoencephalopathy due to aggressive intrathecal chemotherapy was found. Current therapy for patients with DMLC and its clinical ***problems*** are discussed in relation to our experience in this case.

L12 ANSWER 24 OF 28 MEDLINE
AN 88289199 MEDLINE
DN 88289199
TI Intraventricular gamma-globulin for the management of enterovirus encephalitis.
AU Dwyer J.M.; Erlendsson K
CS Department of Clinical Immunology; Yale University School of Medicine, New Haven, CT.
SO PEDIATRIC INFECTIOUS DISEASE JOURNAL, (1988 May) 7(5 Suppl) S30-3. Ref: 11
Journal code: OXJ. ISSN: 0891-3668.
CY United States
DT Journal Article; (JOURNAL ARTICLE)
General Review, (REVIEW)
(REVIEW OF REPORTED CASES)
LA English
FS Priority Journals
EM 198811
AB Although bacterial infections predominate in patients with hypogammaglobulinaemia, patients who do not produce normal amounts of immunoglobulin also have an increased incidence of viral infections. This is particularly true of infections with enteroviruses. Echovirus encephalitis has been a major ***problem*** for patients with hypogammaglobulinaemia. ***Neurologic*** damage, frequently resulting in death, has been common in such patients. Because there is an obligatory extracellular phase in the ***cell*** to ***cell*** spread of enteroviruses, ***therapy*** with immunoglobulin has been attempted. In certain patients intravenous and intrathecal gammaglobulin has temporarily halted progression of the disease, but no patients have been cured by this approach. In this report we detail treatment of three children with X-linked hypogammaglobulinaemia who had encephalitis caused by echovirus infections. Despite doses of intravenous immunoglobulin that maintained the patient's IgG levels within the normal range, their condition deteriorated in all cases. Treatment with intraventricular immunoglobulin was then tried. In all three cases cerebrospinal fluid protein levels and cell counts returned to normal after this treatment and the echoviruses can no longer be isolated from the cerebrospinal fluid.

in children with ***neuroblastoma*** are needed. A scheme for classifying marrow histological appearances is presented which may prove to be of more value than a simple distinction between 'involved' and 'uninvolved'.

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Follow-up time has ranged from 18 months to 4 years. Omnaya reservoirs were placed into the lateral ventricle of each patient and concentrated (5%) immunoglobulin (Sandoglobulin) was injected into the reservoir on a daily basis. On Days 1 through 7 of the regimen patients were given 120, 300, 450, 510, 540 and 600 mg of IgG, respectively. Patients then received 300 mg daily for periods ranging from 1 week to 1 month. Cultures of cerebrospinal fluid removed from the reservoir were repeatedly analyzed to determine the need for further treatment. Clinically the patients improved markedly. (ABSTRACT TRUNCATED AT 250 WORDS)

L12 ANSWER 25 OF 28 MEDLINE
AN 88282438 MEDLINE
DN 88282438
TI Augmentation of cell number and LAK activity in peripheral blood mononuclear cells activated with anti-CD3 and interleukin-2. Preliminary results in children with acute lymphocytic leukemia and ***neuroblastoma***
AU Anderson P.M.; Bach F.H.; Ochoa A.C
CS Immunobiology Research Center; University of Minnesota, Minneapolis 55455.
NC T32CA09445 (NCI)
AI17687 (NIADDK)
AI118326 (NIADDK)
+ SO CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1988) 27(1) 82-8.
Journal code: CN3. ISSN: 0340-7004.
CY GERMANY, WEST; Germany, Federal Republic of
DT Journal Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198811
AB A wide variety of human cancers currently have no effective treatment and are potential targets for lymphokine-activated killer (LAK) cellular immunotherapy. Relapsed acute lymphocytic leukemia (ALL) and ***neuroblastoma*** are two of the major therapeutic challenges in pediatric oncology today. However, one ***problem*** which makes LAK immunotherapy in children particularly difficult is obtaining the large numbers of ***cells*** required. Present adult ***therapeutic***
LAK protocols have utilized short-term (5 day) cultures of interleukin-2 (IL-2)-activated cells which are initially obtained from

leukopheresis.

Since routine use of this procedure in small children is not practical, we have investigated a different approach to obtain increased cell numbers by activation of peripheral blood mononuclear cells with OKT3, a mitogenic anti-CD3 monoclonal antibody, and IL2. Cell growth and LAK activity in OKT3 + IL2-activated cultures were compared to cultures activated with IL2 alone in 2 children with relapsed ALL and 2 children with stage IV ***neuroblastoma***. OKT3 + IL2-activated cultures had marked increases in cell number after 14 days the OKT3 + IL2-activated cultures yielded an approximately 500-fold increase in cell number compared to a 7-fold increase for cultures activated with IL2 alone. In vitro 51Cr release assays were used to estimate LAK activity of the cultures at 7 and 14 days. When tested against HL60, a natural killer (NK)-resistant tumor cell line, not only were total cytolytic units greatly increased in OKT3 + IL2-stimulated cultures by lytic activity on a per cell basis (lytic units/1 x 10(6) cells) had also markedly increased on day 14 of culture.

Phenotypic analysis demonstrated that 80% to 90% of cells in OKT3 + IL2-stimulated cultures were CD3 + T cells. Variable low percentages of CD16 + NK cells were seen in these cultures. In summary, OKT3 + IL2 activation resulted in a large increase in cell yield and the development of high level LAK activity using peripheral blood mononuclear cells from children with cancer. This approach may facilitate the utilization of increased cell numbers in future adoptive immunotherapy protocols, especially in pediatric patients.

L12 ANSWER 26 OF 28 MEDLINE
AN 87089581 MEDLINE
DN 87089581
TI ***Neuroendocrine*** aspects of pineal tumors.
AU Fatell M R; Stein B M
SO NEUROLOGIC CLINICS. (1986 Nov) 4 (4) 877-905.
Journal code: NEU. ISSN: 0733-8619.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198704
AB The evaluation and treatment of pineal region tumors has changed dramatically in the past decade. New imaging techniques result in

earlier

diagnosis. Surgical techniques now permit removal of benign tumors (about one third of cases). Pathologic diagnosis is obtained for the remainder, and postoperative ***therapy*** can be planned rationally. Germ ***cell*** tumors pose a particularly difficult ***problem*** for the pathologist because they often contain mixed germ cell elements.

Biologic markers, beta HCG and AFP, aid diagnosis and can be monitored in serum and CSF to assess response to treatment. Only boys develop precocious puberty with pineal tumors. What appears to be puberty is actually pseudoprecocious puberty, due to ectopic production of HCG by their neoplasms (choriocarcinomas or germinomas with syncytiotrophoblastic giant cells). HCG can stimulate tests to produce testosterone, but FSH is necessary (together with LH or HCG) to stimulate ovaries to produce estrogen. Diabetes insipidus, with pineal tumors is usually due to spread to the hypothalamus by ventricular seeding, but we report a case of aqueductal stenosis with diabetes insipidus resulting from a massively dilated third ventricle. Rarely, hydrocephalus may trigger true precocious puberty, a syndrome easily differentiated from pseudoprecocious puberty by endocrinologic tests. There are no biologic markers to diagnose pineal parenchymal tumors. Elevation of melatonin in plasma or CSF and increased tumor biosynthetic activity has been reported in isolated cases, but the range of melatonin values in normals is very wide, and melatonin levels do not correlate with specific pathologic tumor types. Both parenchymal and nonparenchymal tumors may increase melatonin nonspecifically by interfering with regulatory mechanisms of the normal pineal gland.

L12 ANSWER 27 OF 28 MEDLINE
AN 84304245 MEDLINE
DN 84304245
TI Long-term survival and toxicity in small cell lung cancer. Southwest Oncology Group study.
AU Livingston R B; Stephens R L; Bonnet J D; Groza P N; Lehane D E
NC CA-20319 (NCI)
CA-12644 (NCI)
CA-28862 (NCI)

+ SO AMERICAN JOURNAL OF MEDICINE, (1984 Sep) 77 (3) 415-7.
Journal code: AJU. ISSN: 0002-9343.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198412
AB In the first study of combined chemotherapy and radiation ***therapy*** for small ***cell*** lung cancer by the Southwest Oncology Group. 17 patients survived more than five years after treatment was initiated (4.6 percent). Late relapse, or a second primary malignancy three to six years after diagnosis, accounted for death in five of these patients. Late recurrences involved the chest, bone, and liver, none occurred in the central nervous system. Disease-free survival continues in 10 patients (6 percent of those with limited disease and 1 percent of those with extensive-stage diseases) at a minimal follow-up in excess of six years.
One definite case of chronic treatment-related toxicity occurred: congestive cardiomyopathy after 450 mg/m² of doxorubicin, successfully managed with digitalis and diuretics. One severe ***neurologic*** problem. ***problem*** (orthostatic hypotension with preterminal dementia) and two less severe ***neurologic*** complications (occasional falling episodes without documented cause and cerebrovascular accident) may be treatment-related. Progressive pulmonary disability, post-herpetic pain syndromes, organic brain syndrome, and hematologic abnormalities have not been observed to date. Nitrosourea administration and/or co-administration of a nitrosourea or methotrexate during the induction phase of treatment with radiotherapy to the brain may account for the higher incidence of complications observed by others in long-term survivors.
L12 ANSWER 28 OF 28 MEDLINE
AN 82084383 MEDLINE
DN 82084383
TI [Contamination of a glioma by the herpes virus].
AU Ochsner F
SO SCHWEIZER ARCHIV FUR NEUROLOGIE,
NEUROCHIRURGIE UND PSYCHIATRIE, (1981)

129 (1) 19-30.
Journal code: UDS. ISSN: 0036-7273
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 198204
AB The clinical and ***neuropathologic*** descriptions of a glioma in a 65 years old patient, who died 9 days after its subtotal resection, are documented. The post-mortem study of the brain revealed an herpetic encephalitis with its classical topographical distribution. There were numerous eosinophilic inclusion bodies which ultrastructurally were characteristic of herpes simplex virus. The author discusses, with reference to the literature, the exo and endogenous sources of infection, the means of dissemination, the ***problem*** of latency and reactivation of the virus. He proposes the hypothesis that the infection of the glioma cells in this case was most likely related the immature immunity of the ***cells***, corticoid ***therapy*** and surgical resection acting as inducers. The almost complete absence of an inflammatory reaction evokes an opportunistic viral infection in an immunodeficient patient. Inspite of the description by many authors of different particles which have been interpreted as of viral origin in some brain tumours, the hypothesis of an oncogenic action of the herpetic virus is not retained in this particular case, considered as exceptional, of the glioma described herein. The precocious search for HSV antibodies by immunofluorescence and a temporal lobe biopsy in order to establish an early diagnosis are necessities so as to administer as rapidly as possible the specific therapy, adenine-arabinoside.

L8 277 S L4 AND NEURO?/AB,BI
L9 487 S L2 AND NEURO?/AB,BI
L10 66 S L9 AND L1

FILE 'MEDLINE' ENTERED AT 09:30:39 ON 20 SEP 1999
L11 559 S L9
L12 28 S L11 AND (UNPREDICT? OR PROBLEM?)/AB,BI

=>
...Logging off of STN---
=>
Executing the logoff script...
=> LOG Y
COST IN U.S. DOLLARS ENTRY SESSION SINCE FILE TOTAL
FULL ESTIMATED COST SINCE FILE ENTRY SESSION SINCE FILE TOTAL
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
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STN INTERNATIONAL LOGOFF AT 09:38:30 ON 20 SEP 1999

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FILE 'CAPLUS' ENTERED AT 09:21:46 ON 20 SEP 1999
L1 1331380 S REVIEW/DT
L2 7686 S (CELL?)(SA)(THERAP?)/AB,BI
L3 1401 S L1 AND L2
L4 4796 S (CELL?)(3A)(THERAP?)/AB,BI
L5 918 S L4 AND L1
L6 41 S L5 AND ADMINIST?/AB,BI
L7 1 S L6 AND NEURO?/AB,BI